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In re Patent Application of:
Jesper Wengel et al.

Application No.: 10/208,650 Confirmation No.: 3515

Filed: July 29, 2002 Art Unit: 1637

For: OLIGONUCLEOTIDE ANALOGUES Examiner: J. Riley

MS Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

AMENDMENT UNDER 37 C.F.R. §1.312

Applicants respectfully request that the following amendment be entered prior to issuance of the above-captioned application. The present amendment is being filed prior to payment of the issue fee.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 14 of this paper.

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Application No. (if known): 10/208,650 Attorney Docket No.: 49165C3(71994)

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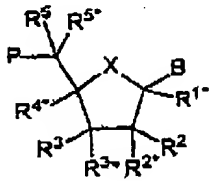
Amendment Under 37 CFR §1.312 (14 pages)

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

157. (previously presented) A nucleoside analogue (hereinafter termed "LNA") of the general formula I



I

wherein X is selected from -O-;

B is selected from hydrogen, hydroxy, optionally substituted C_{1-4} alkoxy, optionally substituted C_{1-4}-alkyl, optionally substituted C_{1-4}-acyloxy, nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

P designates a 5'-terminal group optionally including the substituent R^5;

one of the substituents R^2, R^{2*}, R^3, and R^{3*} is a group P^* which designates an internucleoside linkage or a 3'-terminal group;

one pair of non-geminal substituents R^{4*}, and R^{2*}, designating a biradical selected from the following group:

(a) $-(CR^*R^*)_r-O-(CR^*R^*)_s-$ wherein r is 0 (zero) and s is greater than 1, or s is 0 (zero) and r is greater than 1,

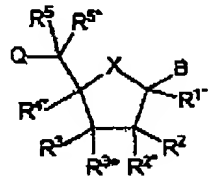
and further wherein each R^* is independently selected from hydrogen, halogen, hydroxy, mercapto, amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA

intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands; and

each of the substituents R^{1*}, R^2, R^3, R^5, and R^{5*}, which are present and not involved in P, P^* is independently selected from hydrogen, optionally substituted C_{1-12}-alkyl, optionally substituted C_{2-12}-alkenyl, optionally substituted C_{2-12}-alkynyl, hydroxy, C_{1-12}-alkoxy, C_{2-12}-alkenyloxy, carboxy, C_{1-12}-alkoxycarbonyl, C_{1-12}-alkylcarbonyl, formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, amino-C_{1-6}-alkyl-aminocarbonyl, mono- and di(C_{1-6}-alkyl)amino-C_{1-6}-alkyl-aminocarbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, C_{1-6}-alkanoyloxy, sulphono, C_{1-6}-alkylsulphonyloxy, nitro, azido, sulphanyl, C_{1-6}-alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted;

and basic salts and acid addition salts thereof.

158. (previously presented) A nucleoside analogue (hereinafter LNA) of the general formula II



II

wherein the substituent B is selected from nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

X is selected from -O-;

one of the substituents R^2, R^3, and R^{3*} is a group Q^*;

each of Q and Q^* is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, Act-O-, mercapto, Prot-S-, Act-S-, C_{1-6}- alkylthio, amino, ProtN(R^H)-, Act-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6} -alkoxy, optionally substituted

C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}- alkenyloxy, optionally substituted C_{2-6}- alkynyl, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-, Act-O-CH_2-, aminomethyl, Prot-N(R^H)-CH_2-, Act-N(R^H)-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -NH(R^H), respectively, Act is an activation group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl;

wherein R^{2*} and R^{4*} together designate a biradical selected from the following group:

(a) $-(CR^*R^*)_r-O-(CR^*R^*)_s-$ wherein r is 0 (zero) and s is greater than 1, or s is 0 (zero) and r is greater than 1,

and further wherein each R^* is independently selected from hydrogen, halogen, hydroxy, mercapto, amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands; and

each of the substituents R^{1*}, R^2, R^3, R^5, and R^{5*}, which are not involved in Q, Q^*, is independently selected from hydrogen, optionally substituted C_{1-12} -alkyl, optionally substituted C_{2-12} - alkenyl, optionally substituted C_{2-12} -alkynyl, hydroxy, C_{1-12} -alkoxy, C_{2-12} -alkenyloxy, carboxy, C_{1-12} -alkoxycarbonyl, C_{1-12} alkylcarbonyl, formyl, aryl, aryloxy-carbonyl, aryloxy, arylcarbonyl, heteroaryl, heteroaryloxy-carbonyl, heteroaryloxy, heteroarylcarbonyl, amino, mono- and di(C_{1-6} - alkyl)amino, carbamoyl, mono- and di(C_{1-6} - alkyl)-amino-carbonyl, amino-C_{1-6} - alkylaminocarbonyl, mono- and di(C_{1-6} - alkyl)amino- C_{1-6} -alkyl-aminocarbonyl, C_{1-6} alkylcarbonylamino, carbamido, C_{1-6} alkanoyloxy, sulphono, C_{1-6} - alkylsulphonyloxy, nitro, azido, sulphanyl, C_{1-6} - alkylthio, halogen, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, where aryl and heteroaryl may be optionally substituted;

and basic salts and acid addition salts thereof;

with the proviso that,

any chemical group (including any nucleobase), which is reactive under the conditions prevailing in oligonucleotide synthesis, is optionally functional group protected.

159 (previously presented). A nucleoside analogue according to claim 158, wherein the group B is selected from nucleobases and functional group protected nucleobases.

160 (previously presented). A nucleoside analogue according to any of the claims 158-159, wherein each of the substituents R^{1*}, R^2, R^3, R^{3*}, R^5, and R^{5*}, which are present and not involved in Q, Q^*, is independently selected from hydrogen, optionally substituted C_{1-6} - alkyl, optionally substituted C_{2-6} - alkenyl, hydroxy, C_{1-6} - alkoxy, C_{2-6},- alkenyloxy, carboxy, C_{1-6} - alkoxycarbonyl, C_{1-6} - alkylcarbonyl, formyl, amino, mono- and di(C_{1-6} - alkyl)amino, carbamoyl, mono- and di(C_{1-6} - alkyl)-amino-carbonyl, C_{1-6}- alkylcarbonylamino, carbamido, azido, C_{1-6} - alkanoyloxy, sulphono, sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, and halogen, and where R^{N*}, when present and not involved in a biradical, is selected from hydrogen and C_{1-6} -alkyl, with the proviso that any hydroxy, amino, mono(C_{1-6} - alkyl)amino, sulfanyl, and carboxy is optionally protected.

161 (previously presented). A nucleoside analogue according to any of the claims 158, 159, each of the substituents R^{1*}, R^2,R^3, R^{3*},and R^5, R^{5*}, which are present and not involved in Q^* designate hydrogen.

162 (previously presented). A nucleoside analogue according to any of the claims 158, 159, wherein R^{3*} designates P^*.

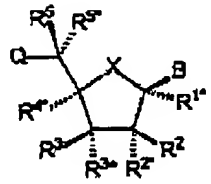
163 (previously presented). A nucleoside analogue according to claim 158, wherein Q is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, mercapto, Prot-S-, C_{1-6}-alkylthio, amino, Prot-N(R^{H})-, mono- or di(C_{1-6} alkyi)amino,

optionally substituted C_{1-6}- alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}- alkenyl, optionally substituted C_{2-6} alkenyloxy, optionally substituted C_{2-6}- alkynyl, optionally substituted C_{2-6}- alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-,

aminomethyl, Prot-N(R^H)-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl; and

Q^* is selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Act-O-, mercapto, Act-S-, C_{1-6},- alkylthio, amino, Act-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkenyloxy, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-6} alkynyloxy, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, where Act is an activation group for -OH, -SH, and - NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl.

164 (previously presented) A nucleoside analogue according to claim 158, having the general formula IIa



IIa

wherein the substituents Q, B, $R^{1"}$, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, and R^{5*} are as defined in claim 158 provided the nucleoside analogue has a configuration other than α-L.

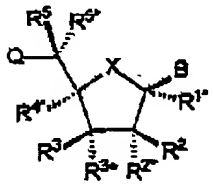
165 (previously presented) A nucleoside analogue according to claim 164, wherein R^{3*} designates P^*.

166. (previously presented) A nucleoside analogue according to claim 165, wherein R^2 selected from hydrogen, hydroxy, and optionally substituted C_{1-6} -alkoxy, and $R^{1"}$, R^3, R^5, and R^{5*}, designate hydrogen.

167. (previously presented) A nucleoside analogue according to any of the claims 165 or 166, wherein B is selected from nucleobases.

168. (previously presented) A nucleoside analogue according to claim 167, wherein B is selected from adenine and guanine thymine, cytosine uracil purine, xanthine, diaminopurine, 8-oxo-N^6-methyladenine, 7-deazaxanthine, 7-deazaguanine, N^4,N^4-ethanocytosin, N^6,N^6-ethano-2,6-diaminopurine, 5-methylcytosine, 5-(C^3-C^6)-alkynylcytosine, 2,6-diaminopyrimidine,2,6-diaminopyrazine,1-methyl-pyrazolo[4,3-d]pyrimidine-5,7(4H,6H)-dione,1-methyl-pyrazolo[4,3-d]pyrimidine-5,7(4H,6H)-dione, 5-fluorouracil, 5-bromouracil, pseudoisocytosine, 2-hydroxy-5-methyl-4-triazolopyridin, isocytosine, isoguanin, and inosine.

169. (previously presented) A nucleoside analogue according to claim 158 of the general formula IIa.



IIa

wherein X is -O-;

B is selected from nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

R^{3*} is a group Q*;

each of Q and Q* is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, Act-O-, mercapto, Prot-S-, Act-S-, C_{1-6}- alkylthio, amino, Prot-N(R^H)-, Act-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands,

carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-, Act-O-CH_2- , aminomethyl, Prot-N(R^H)-CH_2-, Act-N(R^H)-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -NH(R^H), respectively, Act is an activation group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl;

R^{2*} and R^{4*} together designate a biradical selected selected from the following group:

(a) $-(CR^*R^*)_r-O-(CR^*R^*)_s-$ wherein r is 0 (zero) and s is greater than 1, or s is 0 (zero) and r is greater than 1,

and further wherein each R^* is independently selected from hydrogen, halogen, hydroxy, mercapto, amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

each of the substituents R^{1*}, R^2, R^3, R^5, and R^{5*} is independently selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6},-alkenyl, hydroxy, C_{1-6},-alkoxy, C_{2-6},-alkenyloxy, carboxy, C_{1-6}-alkoxycarbonyl, C_{1-6}-alkylcarbonyl, formyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, azido, C_{1-6}-alkanoyloxy, sulphono, sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and halogen; and basic salts and acid addition salts thereof; and with the proviso that any chemical group (including any nucleobase), which is reactive under the conditions prevailing in oligonucleotide synthesis, is optionally functional group protected.

170. (previously presented) A nucleoside analogue according to any of the claim 169, wherein B is selected from nucleobases.

171. (previously presented) A nucleoside analogue according to claim 170, wherein B is selected from adenine and guanine thymine, cytosine uracil purine, xanthine, diaminopurine, 8-oxo-N^6-methyladenine, 7-deazaxanthine, 7-deazaguanine, N^4,N^4-ethanocytosin, N^6,N^6-ethano-2,6-diaminopurine, 5-methylcytosine, 5-(C^3-C^6)-alkynylcytosine, 2,6-diaminopyrimidine,2,6-diaminopyrazine,1-methyl-pyrazolo[4,3-d]pyrimidine-5,7(4H,6H)-dione,1-methyl-pyrazolo[4,3-

d]pyrimidine-5,7(4H,6H)-dione, 5-fluorouracil, 5-bromouracil, pseudoisocytosine, 2-hydroxy-5-methyl-4-triazolopyridin, isocytosine, isoguanin, and inosine.

172. (previously presented). A kit for the isolation, purification, amplification, detection, identification, quantification, or capture of natural or synthetic nucleic acids, the kit comprising a reaction body and one or more LNAs as defined in claim 157.

173. (previously presented) A nucleic acid compound comprising the nucleoside analogue of claim 157.

174. (previously presented) The nucleoside analogue of claim 169, wherein Q* represents an activation group for –OH, -SH, and –NH(R^H).

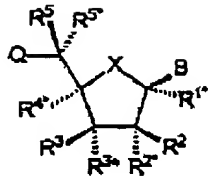
175. (previously presented) The nucleoside analogue of claim 169, wherein said activation group is an optionally substituted phosphoramidite.

176. (previously presented) The nucleoside analogue of claim 169, wherein the nucleoside analogue is a 3'-phosphoramidite derivative.

177. (previously presented) The nucleoside analogue of claim 176, wherein the nucleoside analogue is an O-phosphoramidite.

178. (previously presented) The nucleoside analogue of claim 177, wherein the O-phosphoramidite is N,N-diisopropyl-O-(2-cyanoethyl)phosphoramidite.

179. (previously presented) A nucleoside analogue of the general formula IIa.



IIa

wherein X is -O-;

B is selected from nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

R^{2*} is a group Q*;

each of Q and Q* is independently selected from hydrogen, azido, halogen, cyano, nitro, hydroxy, Prot-O-, Act-O-, mercapto, Prot-S-, Act-S-, C_{1-6}- alkylthio, amino, Prot-N(R^H)-, Act-N(R^H)-, mono- or di(C_{1-6}-alkyl)amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6}-alkenyl, optionally substituted C_{2-6}-alkenyloxy, optionally substituted C_{2-6}-alkynyl, optionally substituted C_{2-6}-alkynyloxy, monophosphate, diphosphate, triphosphate, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, ligands, carboxy, sulphono, hydroxymethyl, Prot-O-CH_2-, Act-O-CH_2- , aminomethyl, Prot-N(R^H)-CH_2-, Act-N(R^H)-CH_2-, carboxymethyl, sulphonomethyl, where Prot is a protection group for -OH, -SH, and -NH(R^H), respectively, Act is an activation group for -OH, -SH, and -NH(R^H), respectively, and R^H is selected from hydrogen and C_{1-6}-alkyl;

R^{2*} and R^{4*} together designate a biradical selected selected from the following group:

(a) –(CR^*R^*)$_r$-O-(CR^*R^*)$_s$ - wherein r is 0 (zero) and s is greater than 1, or s is 0 (zero) and r is greater than 1,

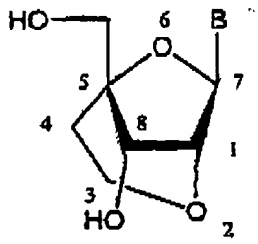
and further wherein each R* is independently selected from hydrogen, halogen, hydroxy, mercapto, amino, optionally substituted C_{1-6}-alkoxy, optionally substituted C_{1-6}-alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands;

each of the substituents R^{1*}, R^2, R^3, R^5, and R^{5*} is independently selected from hydrogen, optionally substituted C_{1-6}-alkyl, optionally substituted C_{2-6},-alkenyl, hydroxy, C_{1-6},-alkoxy, C_{2-6},-alkenyloxy, carboxy, C_{1-6}-alkoxycarbonyl, C_{1-6}-alkylcarbonyl, formyl, amino, mono- and di(C_{1-6}-alkyl)amino, carbamoyl, mono- and di(C_{1-6}-alkyl)-amino-carbonyl, C_{1-6}-alkyl-carbonylamino, carbamido, azido, C_{1-6}-alkanoyloxy, sulphono, sulphanyl, C_{1-6}-alkylthio, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups, and ligands, and halogen;

and basic salts and acid addition salts thereof;

and with the proviso that any chemical group (including any nucleobase), which is reactive under the conditions prevailing in oligonucleotide synthesis, is optionally functional group protected.

180. (previously presented) The nucleoside analogue of claim 157, wherein the analogue is represented by the following structure:



ENA

B = adenine, guanine, thymine, 5-methyl-cytosine, cytosine, uracil, 2,6-diaminopurine

181. (previously presented) The nucleoside analogue of claim 180, wherein the analogue is one of the following specific compounds:

a) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(adenin-9-yl)-2,6-dioxabicyclo[3.2.1]octane,

b) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(guanin-9-yl)-2,6-dioxabicyclo[3.2.1]octane,

c) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(thymin-1-yl)-2,6-dioxabicyclo[3.2.1]octane,

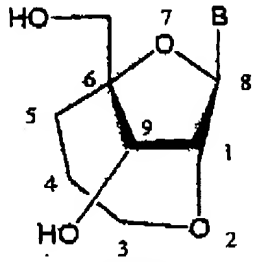
d) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(5-methyl-cytosin-1-yl)-2,6-dioxabicyclo[3.2.1]octane,

e) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(cytosin-1-yl)-2,6-dioxabicyclo[3.2.1]octane,

f) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(uracil-1-yl)-2,6-dioxabicyclo[3.2.1]octane; and

g) (1*R*,5*R*,7*R*,8*S*)-8-hydroxy-5-(hydroxymethyl)-7-(2,6-diaminopurin-9-yl)-2,6-dioxabicyclo[3.2.1]octane.

182. (previously presented) The nucleoside analogue of claim 157, wherein the analogue is represented by the following structure:



Propena

B = adenine, guanine, thymine, 5-methyl-cytosine, cytosine, uracil, 2,6-diaminopurine

Claim 183. (currently amended) The nucleoside analogue of claim ~~182~~ 157, wherein the analogue is one of the following specific compounds:

a) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(adenin-9-yl)-2,5-dioxabicyclo[2.2.1]heptane,

b) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(guanin-9-yl)-2,5-dioxabicyclo[2.2.1]heptane,

c) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(thymin-1-yl)-2,5-dioxabicyclo[2.2.1]heptane,

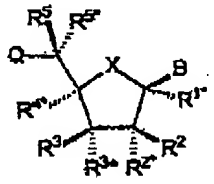
d) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(5-methyl-cytosin-1-yl)-2,5-dioxabicyclo[2.2.1]heptane,

e) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(cytosin-1-yl)-2,5-dioxabicyclo[2.2.1]heptane,

f) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(uracil-1-yl)-2,5-dioxabicyclo[2.2.1]heptane; and

g) (1*R*,3*R*,4*S*,7*R*)-7-hydroxy-1-(hydroxymethyl)-3-(2,6-diaminopurin-9-yl)-2,5-dioxabicyclo[2.2.1]heptane.

184 (previously presented). A nucleoside analogue according to claim 158, having the general formula IIa



IIa

wherein the substituents Q, B, R^{1*}, R^2, R^{2*}, R^3, R^{3*}, R^{4*}, R^5, and R^{5*} are as defined in claim 158 provided the nucleoside analogue has a configuration other than β-D.

185. (previously presented) A method of preparing an LNA modified oligonucleotide (an oligomer) comprising making the oligonucleotide with the LNA of Claim 157.

186 (previously presented) The method of claim 185, wherein the LNA modified oligonucleotide comprises normal nucleosides.

187 (previously presented). A nucleoside analogue according to claim 160, wherein each of the substituents R^{1*}, R^2,R^3, R^{3*},and R^5, R^{5*}, which are present and not involved in Q^* designate hydrogen.

188 (previously presented). A nucleoside analogue according to claim 160, wherein R^{3*} designates P^*.

189 (previously presented). A nucleoside analogue according to claim 161, wherein R^{3*} designates P^*.

REMARKS

Applicants request that the present amendment under 37 CFR §1.312 be entered prior to issuance of the above-captioned patent application. The amendment is intended to address an inadvertent typographical error. Specifically, Applicants have amended claim 183 to change dependency from 182 to claim 157. The amendment is not intended to address any matter related to patentability.

Applicants believe that no fee is required to consider and enter the instant amendment. However, if for any reason a fee is deemed necessary, the USPTO is hereby authorized and requested to charge Deposit Account No. 04-1105 for such fee.

Dated: December 20, 2004

Respectfully submitted,

By _____

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U.S. PATENT DOCUMENTS

Exam. Initials*	Cite No[1]	Document Number	Kind Code[2]	Name of Patentee or Applicant	Publication Date MM-DD-YYYY	Relevant Portion
		6,670,461	B1	WENGEL et al.	12-30-2003	
		2002/0068708	A1	WENGEL et al.	06-06-2002	
		2003/0134808	A1	WENGEL et al.	07-17-2003	
		2003/0144231	A1	WENGEL et al.	07-31-2003	

FOREIGN PATENT DOCUMENTS

Exam Initials*	Cite No[1]	Office[3]	Document Number[4]	Kind Code[5]	Name of Patentee or Applicant	Publication Date MM-DD-YYYY	Relevant Portion	T[6]

Examiner Signature		Date Considered	

* EXAMINER: Initial if document considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number. [2] See kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Place a check here if English translation is attached.

DATE MAILED: AUGUST 17, 2004

Docket No.: 01376CIP/HG
Ser. No. : 09/925,673
Applicants: Masakatsu KANEKO et al.

RECEIPT ACKNOWLEDGED:
REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL (in duplicate); AMENDMENT; INFORMATION DISCLOSURE STATEMENT; FORM PTO/SB/08A AND COPIES OF PUBLS. IDENTIFIED THEREIN; REQUEST FOR ACKNOWLEDGMENT OF (1) APPLICANTS' CLAIM FOR PRIORITY UNDER 35 USC 119 AND ( ) RECEIPT CERTIFIED COPY OF PRIORITY DOCUMENT; CHECKS 5770 (RCE FILING FEE, CHECK NO. 95338) AND 586 (EXTRA IND. CLAIM, CHECK NO. 95339)

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